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Organic Reactions at Alumina Surfaces. Mild and Selective Opening of Arene and Related Oxides by Weak Oxygen and Nitrogen Nucleophiles

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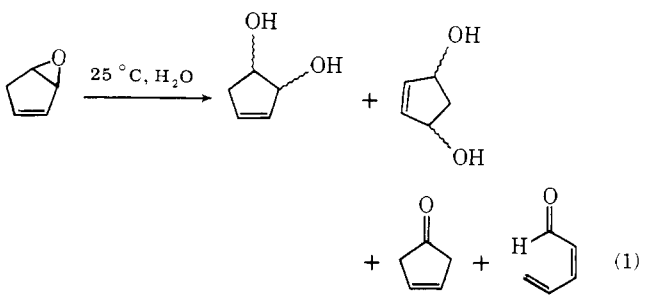
Abstract: Commercially available Woelm 200 basic chromatographic alumina selectively catalyzes the trans opening of both K-region and non-K-region arene oxides by a few equivalents of weak, nonpolarizable oxygen and nitrogen nucleophiles under very mild conditions (25 °C, diethyl ether). Under these conditions nucleophile incorporation competes favorably with aromatization to the corresponding phenol. Vinylic and aryl epoxides are also opened stereo- and regiospecifically by a few equivalents of nucleophiles on neutral alumina.

Metabolism of aromatic hydrocarbons is thought to proceed via arene oxides,[1] and the cytotoxic, mutagenic, and carcinogenic effects of certain polycyclic arenes have been attributed to the covalent binding of the intermediate epoxides to critical cellular macromolecules.[1,2] Much interest, therefore, has been generated concerning the solution chemistry of arene oxides.[3] Recent reports have dealt with the mechanistic details of arene oxide hydrolysis[4] and opening by various nucleophiles;[5] generally, simple arene oxides have been found to undergo aromatization faster than attack by nonpolarizable oxygen and nitrogen nucleophiles.[3] In the accompanying articles, we report that commercially available Woelm 200 chromatographic alumina catalyzes the opening of aliphatic epoxides by a few equivalents of alcohols, thiols, amines, acetic acid, and benzeneselenol.[6] We describe here our finding that this alumina catalyzes trans opening of vinylic epoxides, aryl epoxides, and both K-region and non-K-region arene oxides by a few equivalents of alcohols and amines within 1 h at room temperature.

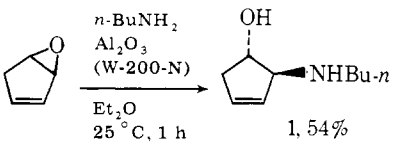
Results and Discussion

Vinylic and Aryl Epoxides. To explore some acid-sensitive and relatively labile oxiranes, we chose two vinylic (cyclopentadiene monooxide and 1,3-cyclohexadiene monooxide) and one aryl epoxide (indene oxide). All three of these epoxides are unusual in that their hydrolysis proceeds via an acid-independent as well as an acid-dependent mechanism.[7] For cyclopentadiene monooxide this acid-independent mechanism leads to rearrangment products as well as diols (eq 1).[8]



(1)

The reactions of cyclopentadiene monooxide with diethyl ether slurries of alumina which had been first "doped" with a few equivalents of 1-butanol or acetic acid gave a mixture of many products. Thus, in the 1-butanol and acetic acid doping the rate of rearrangement appears to be faster than that of nucleophilic attack. In contrast, *n*-butylamine doped alumina was successful in opening the epoxide (eq 2). This success



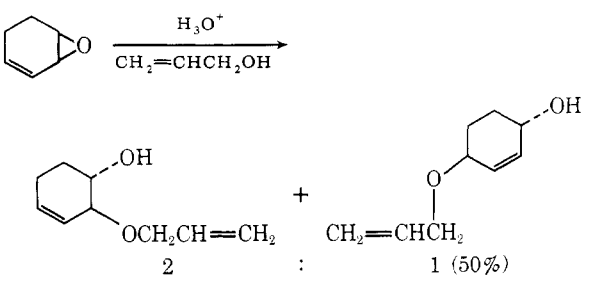
1, 54%

(2)

might be attributed to occupation by the *n*-butylamine of the most acidic sites of the alumina with concomitant reduction in the rate of vinylic epoxide rearrangement.

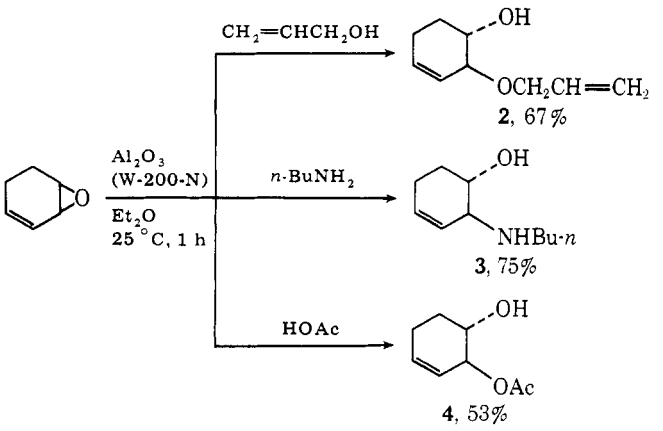
β-Hydroxy amine **1** was the only product isolated from the reaction shown in eq 2. The regiochemistry of hydroxy amine **1** was assigned from its NMR spectrum, which showed no allylic carbinol proton.

1,3-Cyclohexadiene monooxide reacted not only with alumina carrying a few equivalents of allyl alcohol and *n*-butylamine but also with alumina bearing a few equivalents of acetic acid. In each case, only the homoallylic alcohols **2–4** were obtained and were purified in the yields reported in Scheme I. In our hands, pure allyl ether **2** could be prepared in good yield under *vigorous* homogeneous conditions (sodium in refluxing allyl alcohol), but acid-catalyzed reaction with allyl alcohol gave a mixture of 3,4- and 3,6-dioxygenated cyclohexenes as shown in eq 3. *No 3,6-disubstituted cyclohexenes*

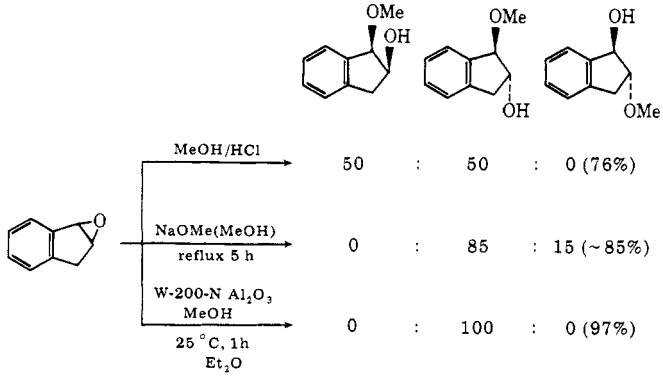


(3)

Scheme I



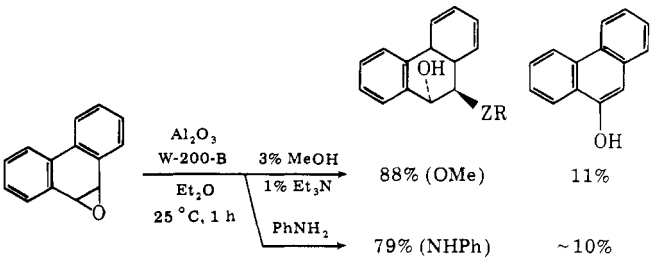
Scheme II



were ever observed in any alumina-promoted opening of cyclohexadiene monooxide.

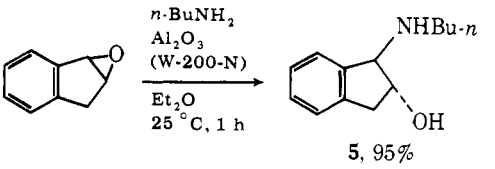
Comparison of homogeneous acid and base and heterogeneous alumina-promoted methanolysis of indene oxide is shown in Scheme II. The alumina reaction was performed by adding indene oxide to a stirring slurry of Woelm W-200-neutral alumina in diethyl ether containing several equivalents of methanol. Stirring for 1 h, methanol extraction, filtration, and evaporation under vacuum gave *trans*-1-methoxy-2-indanol (97%) having spectral properties indentical with those of an authentic sample of this indanol. The trans stereochemistry was assigned based on the NMR coupling constant of the H_1 and H_2 protons (J = 4.2 Hz) and the splitting pattern (two quartets) for the H_2 protons in full agreement with the literature data.[9] The *regiospecific* attachment of the methoxy group at C_1 rather than at C_2 was established by the chemical shift of H_1 (δ 4.4) in contrast to that of H_1 (δ 4.6) observed in an authentic sample of the isomeric *trans*-2-methoxyindanol. The equal mixture of *cis*- and *trans*-1-methoxyindanols formed in the homogeneous acid-catalyzed methanolysis reaction is consistent with a stepwise carbonium ion mechanism with attack of methanol at the electron-deficient benzylic carbon atom.[10] The formation of *trans*-1-methoxy-2-indanol as the major product in the homogeneous base-promoted methanolysis fits a "borderline S_N2" mechanism with epoxide opening electrophilically assisted by methanol and with advanced benzylic carbon–oxygen bond breaking in the transition state leading to products in this synchronous process;[10] the amount of this electrophilic assistance by methanol is probably small because the other regioisomer, *trans*-2-methoxy-1-indanol, is also formed. The Lewis acid sites on alumina[11] apparently also provide electrophilic assistance to opening of indene oxide. The amount of such assistance seems to be slightly greater than that offered by methanol because only *trans*-1-methoxy-2-indanol was formed regiospecifically and

Scheme III



stereospecifically in this heterogeneous reaction; a control experiment showed that had *cis*-1-methoxy-2-indanol been formed (via a benzylic carbonium ion), it would have survived the alumina reaction conditions and would therefore have been detected spectroscopically. If the alumina were acting solely as a base to activate the methanol (i.e., conversion to methoxide),[12] then some of regioisomeric 2-methoxyindanol would have been expected via attack of methoxide at the nonbenzylic epoxide carbon atom. Because of the *mildness, stereospecificity,* and *regiospecificity* of this heterogeneous reaction, it seems possible that the alumina Lewis acid sites activate the epoxide[13] (*with lengthening but probably not complete rupture of the benzylic carbon–oxygen bond*) and that the Lewis base sites *synergistically* activate the methanol.

Reaction of indene oxide with *n*-butylamine-doped alumina likewise gave only *trans*-1-*n*-butylamino-2-indanol (**5**, eq 4).[14]



(4)

5, 95%

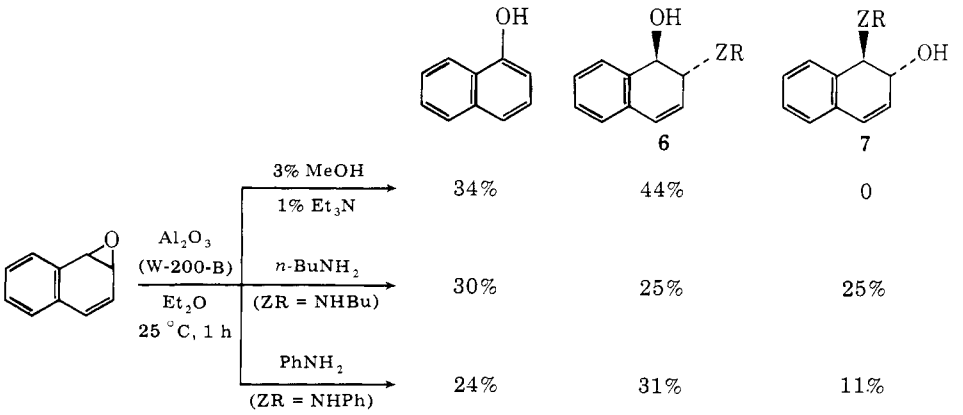
2-Indanone, however, was the major product obtained when indene oxide was treated with acetic acid-doped alumina; such an acid-catalyzed epoxide → ketone rearrangement is typical for indene oxide and other aryl epoxides.

Arene oxides are generally even more susceptible than vinylic or aryl oxiranes to epoxide ring opening and 1,2-hydride shift to give phenols.

Arene Oxides. Phenanthrene 9,10-oxide, a K-region arene oxide, has been opened by a large excess of sodium methoxide in methanol (24 h stirring at room temperature) and by aliphatic amines [50% aqueous tetrahydrofuran, 25 °C (*n*-butylamine) or reflux (*tert*-butylamine) for several hours]; reaction with less nucleophilic amines like aniline has not been reported.[5,15] Using Woelm-200-basic alumina and only several equivalents of nucleophile, we have converted phenanthrene 9,10-oxide selectively and mildly into the corresponding *trans*-methoxy- and *trans*-anilinodihydrophenanthrols (Scheme III, yields of isolated material after purification). Addition of the weak nucleophiles competes favorably with aromatization to phenanthrol. In the methanol-doped alumina reactions, 1% of triethylamine was added to the alumina to reduce the rate of phenanthrol formation relative to the rate of methanol incorporation. The trans stereochemistry was assigned based primarily on the characteristic NMR coupling constant between the H_9 and H_{10} protons (J = 8 Hz).[5c]

Naphthalene 1,2-oxide is at least 250 times more susceptible to spontaneous epoxide ring opening and aromatization than is phenanthrene 9,10-oxide,[3,5c] and opening of this non-K-region arene oxide by nonpolarizable nucleophiles under homogeneous conditions has been reported for methoxide only.[5b] In our hands, a stirring homogeneous diethyl ether solution of naphthalene 1,2-oxide and 5 equiv of aniline at 25 °C for 48 h gave only 1-naphthol. As shown in Scheme IV using Woelm-200-basic alumina and only several equivalents of

Scheme IV



methanol, *n*-butylamine, and aniline, we have transformed naphthalene 1,2-oxide heterogeneously into a mixture of α-naphthol (24–34%) and *trans*-1,2-disubstituted 1,2-dihydronaphthalenes **6** and **7** (42–50%, yields of pure material after chromatographic separation). The regiochemistry and stereochemistry of *trans*-1-hydroxy-2-methoxy-1,2-dihydronaphthalene (**6**, ZR = OMe) were assigned based on the characteristic NMR chemical shifts and coupling constant of the H_1 and H_2 protons which match those values reported in the literature (H_1, δ 4.9; H_2, δ 4.1; $J_{1,2}$ = 10 Hz).[5b,d] The stereochemistry of the amine adducts is less certain but appears to be trans based on the high value of the H_1–H_2 coupling constant ($J_{1,2}$ = 8–10 Hz). The regiochemistry of the aniline adducts **6** and **7** (ZR = NHPh) was assigned tentatively based on the NMR chemical shifts of H_1 and H_2: H_1 δ 4.75 and H_2 δ 4.2 for regioisomer **6** and H_1 δ 4.4 and H_2 δ 4.65 for regioisomer **7.** Aniline adducts **6** and **7** may serve as models for guanine adducts in this system.[16] From these results it is clear that the alumina is effectively increasing the rate of nucleophile incorporation relative to the rate of arene oxide aromatization, since in the absence of alumina 1-naphthol is the only product observed. The trans stereospecificity and the small amount of epoxide rearrangement to naphthol support the general proposal that epoxide opening by RZH-doped alumina is at least in large part a *concerted* process.[13] *Amine-doped alumina is the only method now available for opening naphthalene 1,2-oxide (and probably other non-K-region arene oxides) by weak nitrogen nucleophiles.*

These results are significant because alumina-promoted nucleophilic opening of epoxides is a mild, high-yield, and convenient new synthetic method[6,17] and because opening of arene oxides by weak nucleophiles is considered such a fundamental step in the expression of the toxicological effects of these systems. The important role of the aluminum in these aluminum oxide promoted reactions may have implications for a possible role of a polyvalent metal in some reactions of arene oxides in biological systems.[18]

Experimental Section

Materials. W-200-neutral and basic alumina were purchased from ICN Pharmaceuticals, Cleveland, Ohio. 1,3-Cyclohexadiene monooxide was synthesized by the method of Crandall,[19] indene oxide by the method of Gagio.[20] Cyclopentadiene monooxide was the gift of Professor D. Whalen; phenanthrene 9,10-oxide and naphthalene 1,2-oxide were gifts of Dr. D. M. Jerina. Anhydrous diethyl ether was used as received from Baker. Doping agents were of the best commercially available grade and were distilled from calcium hydride and stored under inert atmosphere (acetic acid excepted).

Methods. Nuclear magnetic resonance spectra were taken on a JEOL MH-100 instrument and are expressed as downfield shifts in parts per million (δ) from tetramethylsilane. Absorptions are characterized as singlets (s), doublets (d), triplets (t), multiplets (m), or broad bands (b). High-pressure liquid chromatography (HPLC) was performed on a Waters Model 6000A liquid chromatography. TLC was done on 20 × 20 cm Analtech plates coated with 1000 μm of silica gel GF. Column chromatography was done with Baker chromatographic grade silica gel (60–200 mesh) used as received.

Melting points were taken on a Mel-Temp melting point apparatus and are uncorrected. Chemical ionization mass spectra were run with ammonia.

General Procedure for Alumina Reactions. A one-neck round-bottom flask equipped with a magnetic stir bar is dried in an oven at ~110 °C for 1 h. The flask is stoppered while hot, allowed to cool, and then tared. The appropriate alumina is then transferred under a dry atmosphere in a glove bag to the flask. The weight of the alumina is determined and enough solvent added to form a slurry. To the stirred slurry is added enough doping agent to equal 4% by weight of the alumina used. Doping agents are measured out by volume (±2%). After 5 min the substrate (1 mmol of epoxide per 7.5 g of alumina, ±5%) is added in 2–3 mL of solvent. After the appropriate amount of time has elapsed, the slurry is poured into 50–100 mL of methanol and allowed to stand for 4 h. The mixture is then filtered through a Celite pad and the solid washed well with methanol. The solvent is removed from the filtrate in vacuo to give the product.

Cyclopentadiene Monooxide on *n*-Butylamine-Doped Alumina. Cyclopentadiene monooxide (0.0840 g, 1.024 mmol) was allowed to react in diethyl ether with 7.679 g of Woelm-200-neutral alumina doped with *n*-butylamine (0.31 g, 4.2 mmol) for 1 h at room temperature. Workup gave 0.1379 g of a solid which was molecularly distilled (100 °C, 0.15 mmHg) to give 0.0863 g (54%) of *trans*-2-*n*-butylamino-3-cyclopenten-1-ol: NMR ($CDCl_3$) δ 0.9 (t, CH_3, 3 H), 1.4 (m, CH_2, 4 H), 2.2 (m, =C-CH_a, 1 H), 2.7 (m, =C-CH_b, 1 H), 2.7 (m, CH_2N, 2 H), 3.1 (s, OH, NH, 2 H), 3.6 (m, CHO, 1 H), 4.1 (m, CHN, 1 H), 5.75 (s, CH=CH, 2 H); IR (thin film) 3580, 3450–3250, 1600, 1065 cm^{-1}. The regiochemistry was assigned on the basis of the downfield shift of the allylic amino carbinol proton. An analytical sample was prepared as the hydrochloride, mp 204–205 °C (ethyl acetate/ethanol). Anal. Calcd for $C_9H_{18}ClNO$: C, 55.86; H, 9.30; N, 7.24. Found: C, 55.97; H, 9.35; N, 7.36.

1,3-Cyclohexadiene Monooxide on Allyl Alcohol Doped Alumina. 1,3-Cyclohexadiene monooxide (0.1546 g, 1.61 mmol) was allowed to react in diethyl ether with 11.421 g of Woelm-200-neutral alumina doped with allyl alcohol (0.46 g, 7.9 mmol) for 1 h at room temperature. Workup gave 0.2131 g of an oil which was molecularly distilled (150 °C, 20 mmHg) to give 0.1667 g (67%) of *trans*-2-allyloxy-3-cyclohexen-1-ol: NMR (CCl_4) δ 1.4–2.2 (b, CH_2 4 H), 3.4 (s, OH, 1 H), 3.6 (m, C*H*OH, 1 H), 3.7 (s, CHOC, 1 H), 4.1 (d, OCH_2C=, 2 H), 5.2 (b, =CH_2, 2 H), 5.9 (m, CH=, 1 H); IR (thin film) 3420, 1645, 1065 cm^{-1}. The regiochemistry was assigned on the basis of the downfield shift of the tertiary ether carbinol. The low-resolution mass spectrum showed no molecular ion. No analytical sample could be obtained owing to the material's instability to preparative VPC.

1,3-Cyclohexadiene Monooxide on Acetic Acid Doped Alumina. 1,3-Cyclohexadiene monooxide (0.1698 g, 1.761 mmol) was allowed to react in diethyl ether with 13.127 g of Woelm-200-neutral alumina doped with acetic acid(0.53 g, 8.8 mmol) for 1 h at room temperature. Workup gave 0.1450 g (53%) of *trans*-2-hydroxy-5-cyclohexenyl acetate: NMR ($CDCl_3$) δ 1.6–2.3 (b, CH_2, 4 H), 2.1 (s, CH_3, 3 H), 3.3 (s, OH, 1 H), 3.8 (m, C*H*OH, 1 H), 5.2 (m, CHOC, 1 H), 5.5 (m, CH=, 1 H), 5.8 (m, =CHCO, 1 H); IR (thin film) 3440, 3030, 1730,

1240, 1030 cm^{-1}; mass spectrum *m/e* 138 (parent, molecular ion −18). The regiochemistry was assigned on the basis of the downfield shift of the acetate carbinol proton.

The acetate was saponified by refluxing in 20 mL of aqueous 8 N potassium hydroxide and 20 mL of methanol for 24 h. The solution was poured into 150 mL of water, and the resulting solution saturated with sodium chloride and extracted continuously with chloroform for 48 h. The organic phase was dried over potassium carbonate and the solvent removed in vacuo to give 0.0899 g of an oil. Trituration with diethyl ether followed by recrystallization (diethyl ether/chloroform) gave 0.0464 g of *trans*-3-cyclohexene-1,2-diol, mp 74.5–76.5 °C (lit.[21] mp 77.5 °C).

1,3-Cyclohexadiene Monooxide on *n*-Butylamine-Doped Alumina. 1,3-Cyclohexadiene monooxide (0.1323 g, 1.378 mmol) was allowed to react in diethyl ether with 9.883 g of Woelm-200-neutral alumina doped with *n*-butylamine (0.40 g, 5.5 mmol) for 1 h at room temperature. Workup gave 0.1992 g of an oil which was molecularly distilled (150 °C, 14 mm) to give 0.1740 g (75%) of *trans*-2-*n*-butylamino-3-cyclohexen-1-ol: NMR ($CDCl_3$ δ 0.9 (t, CH_3, 3 H), 1.4, 2.0 (b, CH_2, 8 H), 2.6 (m, CH_2N, 2 H), 3.0 (m, =CCHN, 1 H), 3.1 (s, OH, NH, 2 H), 3.5 (m, CHO, 1 H), 5.6 (s, CH=CH, 2 H); IR (thin film) 3450–3100, 1650, 1055 cm^{-1}. The regiochemistry was assigned on the basis of the downfield shift of the tertiary amino carbinol proton and the absence of an allylic carbinol proton. An analytical sample was obtained as the hydrochloride, mp 198–201 °C dec (ethyl acetate/ethanol). Anal. Calcd for $C_{10}H_{20}ClNO$: C, 58.39; H, 9.73; N, 6.81. Found: C, 58.24; H, 9.70; N, 6.70.

Indene Oxide on Methanol-Doped Alumina. Indene oxide (0.1154 g, 0.874 mmol) was allowed to react in diethyl ether with 6.361 g of Woelm-200-neutral alumina doped with methanol (0.25 g, 7.8 mmol) for 1 h at room temperature. Workup gave 0.1394 g (97%) of *trans*-1-methoxy-2-indanol: NMR (CCl_4) δ 2.5 (m, $PhCH_a$, 1 H), 3.1 (m, $PhCH_b$, 1 H), 3.35 (s, CH_3, 3 H), 3.8 (m, OH, 1 H), 4.2 (m, C*H*OH, 1 H), 4.4 (d, J = 4.16 Hz, CHOC, 1 H), 7.1 (m, PhH, 4 H); IR (thin film) 3400, 1605, 1070 cm^{-1}. The NMR and IR spectra were identical with those of an authentic sample.

Indene Oxide on *n*-Butylamine-Doped Alumina. Indene oxide (0.1233 g, 0.934 mmol) was allowed to react in diethyl ether with 7.360 g of Woelm-200-neutral alumina doped with *n*-butylamine (0.29 g, 4.0 mmol) for 1 h at room temperature. Workup gave 0.1812 g (95%) of *trans*-1-*n*-butylamino-2-indanol: mp 110–115 °C; NMR ($CDCl_3$) δ 0.9 (t, CH_3, 3 H), 1.4 (m, CH_2, 4 H), 2.8 (b, OH, NH, CH_2N, $PhCH_a$, 5 H), 3.2 (m, $PhCH_b$, 1 H), 4.0 (d, J = 5 Hz, PhCHN, 1 H), 4.3 (m, CHO, 1 H), 7.2 (m, PhH, 4 H); IR ($CHCl_3$) 3600, 3350, 1600, 1065 cm^{-1}. The regiochemistry was assigned on the basis of the downfield shift of the benzylic amino carbinol proton. Recrystallization (chloroform)gave an analytical sample as white needles, mp 117.5–118.5 °C. Anal. Calcd for $C_{13}H_{19}NO$: C, 76.09; H, 9.27; N, 6.83. Found: C, 76.16; H, 9.38; N, 7.25. Mass spectrum *m/e* 205 (parent, molecular ion).

Phenanthrene 9,10-Oxide on Methanol-Doped Alumina. Phenanthrene 9,10-oxide (0.0131 g, 0.068 mmol) was allowed to react in diethyl ether for 1 h at room temperature with 1.671 g of Woelm-200-basic alumina doped with triethylamine (1%, 0.017 g) and methanol (3%, 0.05 g, 1.6 mmol). Workup gave 0.0152 g of an oil. Column chromatography (50:50 diethyl ether/petroleum ether) on 1.9 g of silica gel gave 0.0015 g (11%) of 9-phenanthrol and 0.0135 g (88%) of *trans*-9,10-dihydro-10-methoxy-9-phenanthrol: NMR ($CDCl_3$) δ 2.25 (m, OH, 1 H), 3.6 (s, OCH_3, 3 H), 4.35 (d, $J_{a,b}$ = 8 Hz, CH_aOC, 1 H), 4.85 (d, CH_bOH, 1 H), 7.3–7.85 (b, PhH, 8 H). Reported values[5c] H_a 4.38, H_b 4.87, $J_{a,b}$ = 8 Hz. IR ($CHCl_3$) 3595, 3440, 3070 cm^{-1}.

Phenanthrene 9,10-Oxide on Aniline-Doped Alumina. Phenanthrene 9,10-oxide (0.0292 g, 0.151 mmol) was allowed to react in diethyl ether with 2.069 g of Woelm-200-basic alumina doped with aniline (0.083 g, 0.89 mmol) for 1 h at room temperature. Workup gave 0.0455 g of a solid. Column chromatography on 7 g of silica gel)50:50 diethyl ether/petroleum ether) gave 0.0078 g of a mixture of 9-phenanthrol and the product and 0.0341 g (79%) of *trans*-9,10-dihydro-10-phenylamino-9-phenanthrol: NMR ($CDCl_3$) δ 4.6 (distorted doublets, J = 10 or 15 Hz, CHN, CHO, 2 H), 6.6, 7.0–7.7 (b, PhH, 13 H); IR ($CHCl_3$) 3580, 3400, 1600, 1005 cm^{-1}. Recrystallization from hexane/ethyl acetate gave 0.0067 g of fluffy needles, mp 143–144 °C. Chemical ionization mass spectroscopy showed a base peak of *m/e* 288 (molecular ion plus 1).

Naphthalene 1,2-Oxide on Methanol-Doped Alumina. Naphthalene 1,2-oxide (0.0367 g, 0.2555 mmol) was allowed to react in diethyl ether for 1 h at room temperature with 2.634 g of Woelm-200-basic alumina doped with triethylamine (1%, 0.026 g) and methanol (3%, 0.079 g, 2.5 mmol). Workup gave 0.0456 g of a solid. Column chromatography on 7 g of silica gel (50:50 diethyl ether/petroleum ether) gave 0.0126 g (34%) of 1-naphthol and 0.0199 g (44%) of *trans*-1,2-dihydro-2-methoxy-1-naphthol: NMR ($CDCl_3$) δ 2.55 (m, OH, 1 H), 3.45 (s, OCH_3, 3 H), 4.1 (m, CH_aOC, 1 H), 4.9 (d, J_{ab} = 10 Hz, CH_bOH, 1 H), 6.0 (d, =CH, 1 H), 6.4 (d, PhCH=, 1 H), 7.2, 7.5 (b, PhH, 4 H), Reported[5b] values H_a 4.08, H_b 4.90, $J_{a,b}$ = 10.0 Hz. IR ($CDCl_3$) 3590, 3410, 1630, 1595, 1100 cm^{-1}. Mass spectrum *m/e* 176 (parent, molecular ion).

Naphthalene 1,2-Oxide on *n*-Butylamine-Doped Alumina. Naphthalene 1,2-oxide (0.0368 g, 0.255 mmol) was allowed to react in diethyl ether for 1 h at room temperature with 2.547 g of Woelm-200-basic alumina doped with *n*-butylamine (0.14 g, 1.9 mmol). Workup gave 0.0545 g which upon preparative HPLC (Porasil, 4% methanol in chloroform) gave 0.0111 g (30%) of 1-naphthol and 0.0270 g (49%) of a 50:50 mixture of *trans*-1,2-dihydro-2-*n*-butylamino-1-naphthol and *trans*-1,2-dihydro-1-*n*-butylamino-2-naphthol. This mixture could be separated analytically but not preparatively: NMR ($CDCl_3$) δ 0.9 (t, CH_3, 3 H), 1.4 (m, CH_2, 4 H), 3.35 (m, =CCHN, 0.5 H), 3.7 (d, J = 8.5 Hz, PhCHN, 0.5 H), 4.2 (m, =CCHO, 0.5 H), 4.6 (d, J = 10 Hz, PhCHO, 0.5 H), 6.0 (m, =CH, 1 H), 6.45 (m, PhCH=, 1 H), 7.2, 7.5 (b, PhH, 4 H); IR ($CHCl_3$) 3580, 3500–3300, 3050, 1450, 1100, 1040 cm^{-1}. The chemical ionization mass spectrum showed a base peak of *m/e* 218 (molecular ion plus one).

Naphthalene 1,2-Oxide on Aniline-Doped Alumina. Naphthalene 1,2-oxide (0.0835 g, 0.5799 mmol) was allowed to react in diethyl ether for 1 h at room temperature with 12.025 g of Woelm-200-basic alumina doped with aniline (0.45 g, 5.2 mmol). Workup gave 0.1115 g of a solid. Column chromatography on 22 g of silica gel (15:85 ethyl acetate/petroleum ether) gave 0.0204 g (24%) of 1-naphthol, 0.0431 g (31%) of *trans*-1,2-dihydro-2-phenylamino-1-naphthol, mp 134–136 °C dec, and 0.0157 g (11%) of *trans*-1,2-dihydro-1-phenylamino-2-naphthol.

trans-1,2-Dihydro-2-phenylamino-1-naphthol: NMR ($CDCl_3$) 2.9 (b, NH, OH, 2 H), 4.2 (m, CHN, 1 H), 4.75 (d, J = 8 Hz, CHO 1 H), 5.9 (m, =CHCN, 1 H), 6.5 (d, PhCH=, 1 H), 6.6, 7.1 (m, PhH, 9 H); IR ($CHCl_3$) 3570, 3410, 1600, 1500, 995 cm^{-1}. The chemical ionization mass spectrum showed a base peak of *m/e* 238 (molecular ion plus one). Three recrystallizations from benzene gave an analytical sample. Anal. Calcd for $C_{16}H_{15}NO$: C, 81.01; H, 6.33; N, 5.91. Found: C, 81.46; H, 6.19; N, 5.83.

trans-1,2-Dihydro-1-phenylamino-2-naphthol: NMR ($CDCl_3$) δ 3.4–3.9 (b, OH, NH, 2 H), 4.4 (d, CHN, 1 H), 4.65 (d, J = 10 Hz, CHO, 1 H), 6.0 (m, =CHCO, 1 H), 6.4 (d, PhCH=, 1 H), 6.7 (m, PhH, 2 H), 7.1 (m, PhH, 7 H); IR ($CHCl_3$) 3570, 3405, 1600, 1500, 1050 cm^{-1}. The chemical ionization mass spectrum showed a base peak of *m/e* 238 (molecular ion plus one).

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Selective Reductions. 24. Acyloxyboranes in the Controlled Reaction of Carboxylic Acids with Borane–Tetrahydrofuran. Acyloxyboranes as Intermediates in the Fast Reduction of Carboxylic Acids by Borane–Tetrahydrofuran

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Abstract: The controlled reaction of carboxylic acids with borane-THF at appropriate temperatures makes available mono-, di-, and triacyloxyboranes, RCO_2BH_2, $(RCO_2)_2BH$, and $(RCO_2)_3B$. A number of these have been synthesized and characterized. The first unambiguous examples of triacyloxyboranes have been isolated and characterized. A number of addition compounds of tetrahydrofuran with diacyloxyboranes have been prepared. Finally, a relatively stable monoacyloxyborane has been identified, as well as less stable monoacyloxyboranes, possible intermediates in the reduction of carboxylic acid. Treatment of the carboxylic acids with borane-THF (1:1), the diacyloxyborane with borane-THF, or the triacyloxyborane with borane-THF (1:2) produces at the same rate the corresponding trialkoxyboroxines (readily hydrolyzed to the alcohols). These results establish that the extraordinarily fast reduction of carboxylic acids by borane-THF must proceed through the intermediate formation of monoacyloxyborane, either formed directly from the carboxylic acid and borane, or formed by a redistribution reaction of diacyloxyborane with borane.

We have recently described the remarkable ease with which carboxylic acids, both aliphatic and aromatic, are reduced by borane-tetrahydrofuran.[2,3] However, acyloxyboranes, proposed intermediates in these reductions, have never been carefully characterized or explored. Consequently, the precise mechanism of the reduction is not well understood.

The only system which has been repeatedly explored is triacetoxyborane (**1**), reportedly synthesized by a variety of procedures (eq 1).[4-6]

$$\begin{array}{l} \tfrac{1}{2}B_2O_3 + \tfrac{3}{2}(CH_3CO)_2O \\ B(OH)_3 + 3(CH_3CO)_2O \\ BCl_3 + 3CH_3CO_2H \end{array} \xrightarrow[-3HCl]{-3HOAc} \underset{\mathbf{1}}{(CH_3CO_2)_3B} \quad (1)$$

Other workers using these procedures have reported the product to be not **1**, but rather, oxybis(diacetoxyborane) (**2**), presumably formed in the dismutation of **1** (eq 2, R = CH_3).[7-9]

$$2(RCO_2)_3B \rightarrow \underset{\mathbf{2}}{(RCO_2)_2BOB(O_2CR)_2} + (RCO)_2O \quad (2)$$

The reaction of carboxylic acids with borane-THF is remarkably clean.[2] If the subsequent reduction of the intermediates could be controlled, this reaction offered promise of providing a new, very mild general route to triacyloxyborane, $(RCO_2)_3B$, and possibly to the intermediate derivatives, diacyloxyborane, $(RCO_2)_2BH$, and monoacyloxyborane, RCO_2BH_2. Accordingly, we undertook a study of the reaction of representative carboxylic acids with borane-THF under mild, controlled reaction conditions.

Results and Discussion

Stoichiometry of the Reaction of Carboxylic Acids with Borane-THF. The reduction of carboxylic acids by borane-